Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 DEC 2004 HIGHEST RN 798532-74-8
DICTIONARY FILE UPDATES: 15 DEC 2004 HIGHEST RN 798532-74-8

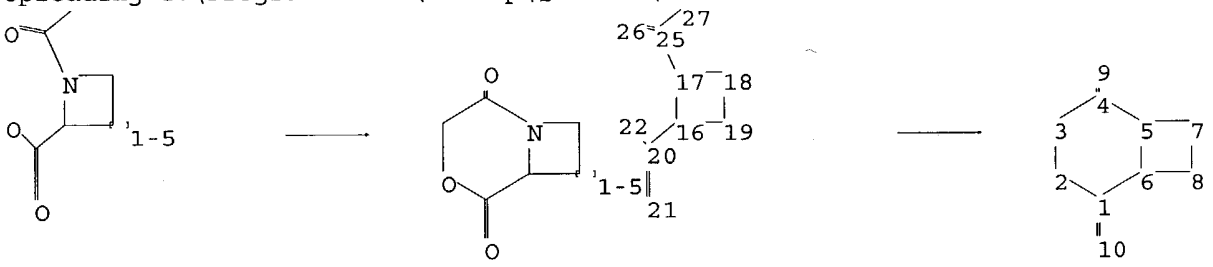
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10695048aaa.str

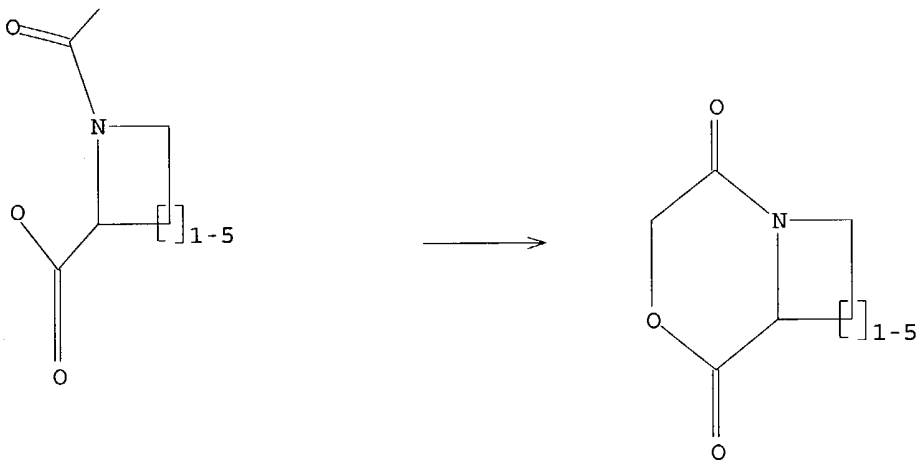


chain nodes :
9 10 20 21 22 25 26 27
ring nodes :
1 2 3 4 5 6 7 8 16 17 18 19
chain bonds :
1-10 4-9 16-20 17-25 20-21 20-22 25-26 25-27
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-8 7-8 16-17 16-19 17-18 18-19
exact/norm bonds :
1-2 1-6 1-10 2-3 3-4 4-5 4-9 5-6 5-7 6-8 7-8 16-17 16-19 17-18 17-25
18-19 20-21 20-22 25-26
exact bonds :
16-20 25-27
isolated ring systems :
containing 1 : 16 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS 22:CLASS 25:CLASS
26:CLASS 27:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 16

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> file casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.42	0.63

FILE 'CASREACT' ENTERED AT 14:45:41 ON 17 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTENT:1840 - 12 Dec 2004 VOL 141 ISS 24

****
*
* CASREACT now has more than 8 million reactions *
*
****

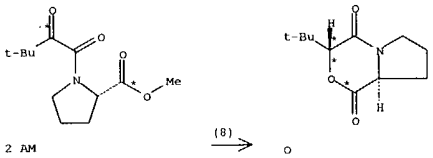
Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

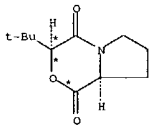
```
=> s l1
SAMPLE SEARCH INITIATED 14:45:48 FILE 'CASREACT'
SCREENING COMPLETE -     38 REACTIONS TO VERIFY FROM      1 DOCUMENTS

100.0% DONE     38 VERIFIED       0 HIT RXNS                     0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:       391 TO     1129
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1 (     0 REACTIONS)

=> s l1 sss full
FULL SEARCH INITIATED 14:45:55 FILE 'CASREACT'
SCREENING COMPLETE -   1293 REACTIONS TO VERIFY FROM     44 DOCUMENTS

100.0% DONE   1293 VERIFIED      46 HIT RXNS                    15 DOCS
SEARCH TIME: 00.00.01

L3           15 SEA SSS FUL L1 (    46 REACTIONS)

=> d fhit ibib abs tot
```

L3 ANSWER 1 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(8) OF 129 ...2 AM ===> O + AN...



2 AM (8) O YIELD 67%(93)



AN
YIELD 67%(7)

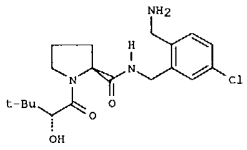
RX(8) RCT AM **259173-97-2**

STAGE(1)
CAT 7440-18-8 Ru
SOL 67-56-1 MeOH

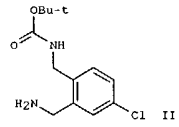
STAGE(2)
RGT I 1333-74-0 H2

STAGE(3)
RGT AK 104-15-4 TsOH
SOL 108-88-3 PhMe
PRO O **685876-05-5**, AN 714237-96-4
NTE stereoselective

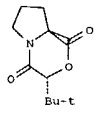
ACCESSION NUMBER: 141:88980 CASREACT
TITLE: Stereoselective Synthesis of a Potent Thrombin Inhibitor by a Novel P2-P3 Lactone Ring Opening
AUTHOR(S): Nelson, Todd D.; LeBlond, Carl R.; Frantz, Doug E.; Matty, Louis; Mitten, Jeffrey V.; Weaver, Damian G.; Moore, Jeffrey C.; Kim, Jaehon M.; Boyd, Russell; Kim, Pei-Yi; Gbewonyo, Kodzo; Brower, Mark; Sturr, Michael; McLaughlin, Kathleen; McMasters, Daniel R.; Kress, Michael H.; McNamara, James M.; Dolling, Ulf H.
CORPORATE SOURCE: Department of Process Research, Merck Research Laboratories, Merck & Co., Wayne, PA, 19087, USA
SOURCE: Journal of Organic Chemistry (2004), 69(11), 3620-3627
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



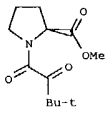
I



II



III



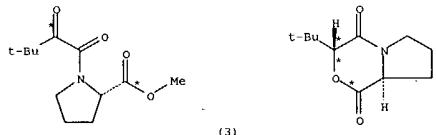
IV

AB The concise synthesis of a potent thrombin inhibitor I·HBr was accomplished by a mild lactone aminolysis between an orthogonally protected bis-benzylic amine II and a diastereomerically pure lactone III. The lactone was synthesized by the condensation of L-proline Me ester with an enantiomerically pure 2-hydroxy-3,3-dimethylbutanoic acid, which in turn was synthesized by a highly stereoselective (>500:1 er) and productive (100000:1, S/C) enzymic reduction of corresponding α-ketoester followed by hydrolysis. In addition, a second route to the enantiomerically pure lactone III was accomplished via diastereoselective reduction of ketoamide IV.
REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS

L3 ANSWER 1 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(3) OF 5 ...C ===> J



C (3) J YIELD 67%

own work

RX(3) RCT C **259173-97-2**

STAGE(1)
RGT G 1333-74-0 H2
CAT 7440-18-8D Ru
SOL 67-56-1 MeOH

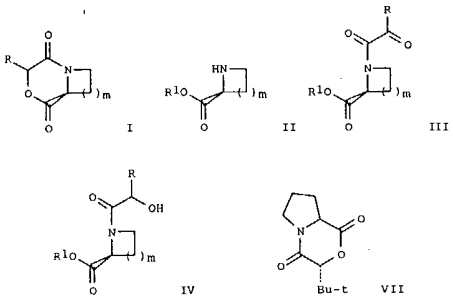
STAGE(2)
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe
PRO J **685876-05-5**
NTE second stage stereoselective, other product detected

ACCESSION NUMBER: 140:391288 CASREACT
TITLE: Process of making N-heterocyclic bicyclic lactone compounds from ketoamides
INVENTOR(S): Nelson, Todd D.; Leblond, Carl; Mitten, Jeffrey V.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004087790	A1	20040506	US 2003-695048	20031028
PRIORITY APPLN. INFO.:			US 2002-422701P	20021031

OTHER SOURCE(S): MARPAT 140:391288
GI

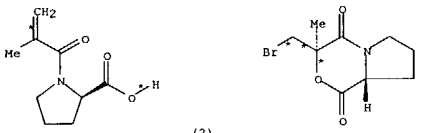
L3 ANSWER 2 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



AB Disclosed is a process of preparing a fused morpholine-2,5-dione [I; wherein
R is (a) C 1-6 alkyl unsubstituted or substituted with one, two, or three groups independently selected from C 6-10 aryl, C 1-6 alkoxy, halogen, and
amino; or (b) a 6-10 membered monocyclic or bicyclic aryl ring system, unsubstituted or substituted with one, two or three groups independently selected from C1-6 alkyl, C1-6 alkoxy, halogen, and amino group; and m is 1, 2, 3, 4, or 5] which comprises coupling a keto acid of formula RCOCO2H (R = same as above) with 1-azacycloalakane-2-carboxylic acid ester [II; R1
= (a) C1-6 alkyl unsubstituted or substituted with 1 to 3 groups independently selected from C6-10 aryl, HO, C1-6 alkoxy, halogen, and amino, (b) benzyl unsubstituted or substituted with one, two or three groups independently selected from C1-6 alkyl, hydroxy, C1-6 alkoxy, halogen, and amino, or (c) hydrogen], reducing the resulting ketoamides (III; R, R1, m = same as above), and cyclization of the resulting hydroxy ketoamides (IV; R, R1, m = same as above). Thus, 3,3-dimethyl-2-oxobutanoic acid was coupled with L-proline Me ester hydrochloride using HOBt/EDC as coupling reagents to give N-(3,3-dimethyl-2-oxobutanoyl)-L-proline Me ester (V) which was hydrogenated over 5% Ru/C in methanol at 50° and 40 psig H pressure for 71 h to give a crude mixture of N-((R)- and (S)-3,3-dimethyl-2-hydroxybutanoyl)-L-proline Me ester (VI). VI was dissolved in toluene and stirred in the presence of p-MeC6H4SO3H at
room temperature for 3 h under reduced pressure with removing methanol formed to
give, after silica gel chromatog., lactone (VII) in 67% yield from V.

L3 ANSWER 3 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 15 ...C ===> G...



C (2) G
YIELD 81%

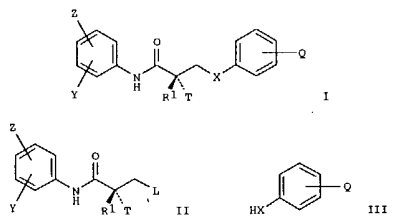
RX(2) RCT C **106089-24-1**
RGT H 128-08-5 Bromosuccinimide
PRO G **106138-80-1**
SOL 68-12-2 DMF
NTE bromination and cyclization

ACCESSION NUMBER: 140:111132 CASREACT
TITLE: Method for preparation of N-[4-nitro-3-(trifluoromethyl]phenyl]-(2S)-3-[4-(acetylamino)phenoxy]-2-hydroxy-2-methylpropanamide and related compounds as selective androgen receptor modulators
INVENTOR(S): Dalton, James T.; Miller, Duane D.; He, Yali; Yin, Donghua
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 935,044.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014975	A1	20040122	US 2002-277108	20021022
US 2002099036	A1	20020725	US 2001-935044	20010823
US 6492554	B2	20021210		
US 2002099096	A1	20020725	US 2001-935045	20010823
US 6569896	B2	20030527		
PRIORITY APPLN. INFO.:			US 2000-367355P	20000824
			US 2000-644970	20000824
			US 2001-300083P	20010625
			US 2001-935044	20010823
			US 2001-935045	20010823

OTHER SOURCE(S): MARPAT 140:111132
GI

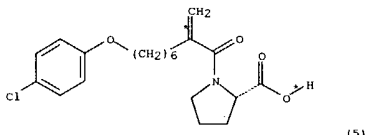
L3 ANSWER 3 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



AB The present invention relates to a synthetic process for the preparation of a
novel class of androgen receptor targeting agents (ARTA) [I; wherein X = O, NH, Se, PR, or NR; T = OH, OR, NHCOMe, NHCOR; Z = NO2, cyano, CO2H, COR, NHCOR, CONHR; Y = CF3, F, I, Br, Cl, cyano, CR3, SnR3; Q = alkyl, halogen, CF3, cyano, CR3, SnR3, NR2, NHCOMe, NHCOCF3, NHCOR, NHCONHR, NHCO2R, OCONHR, CONHR, NHCSMe, NHCSCF3, NHCSR NHSO2Me, NHSO2R, OR, COR, OCOR, OSO2R, SO2R, SR; or Q together with the benzene ring to which it is attached is a fused ring system represented by structure Q1, Q2 or Q3; R =
alkyl, haloalkyl, dihaloalkyl, trihaloalkyl, CH2F, CHF2, CF3, CF2CF3, aryl, Ph, halogen, alkenyl, OH; R1 = Me, CH2F, CHF2, CF3, CH2CH3, CF2CF3] comprising the step of coupling an amide of formula (II) (Z, Y, R1, T = same as above; L = a leaving group) with a compound of formula (III) (Q, X =
same as above). These agents demonstrate androgenic and anabolic activity
of a nonsteroidal ligand for the androgen receptor (no data). The agents define a new subclass of compds. which are selective androgen receptor modulators (SARM) which are useful for (a) male contraception, (b) treatment of a variety of hormone-related conditions, for example conditions associated with androgen decline in aging male (ADAM), such as fatigue, depression, decreased libido, sexual dysfunction, erectile dysfunction, hypogonadism, osteoporosis, hair loss, anemia, obesity, sarcopenia, osteopenia, osteoporosis, benign prostate hyperplasia, alterations in mood and cognition and prostate cancer, (c) treatment of conditions associated with androgen decline in female (ADIF), such as sexual
dysfunction, decreased sexual libido, hypogonadism, sarcopenia, osteopenia, osteoporosis, alterations in cognition and mood, depression, anemia, hair loss, obesity, endometriosis, breast cancer, uterine cancer and ovarian cancer, (d) treatment and/or prevention of chronic muscular wasting, (e) decreasing the incidence of, halting or causing a regression of prostate cancer, and (f) oral androgen replacement and/or other clin. therapeutic and/or diagnostic areas. The process of the present invention
is suitable for large-scale preparation, since all of the steps give highly pure compds., thus avoiding complicated purifn. procedures which ultimately lower the yield. Thus, the present invention provides methods for the synthesis of non-steroidal agonist compds., that can be used for industrial large-scale synthesis, and that provide highly pure products in
high yield.

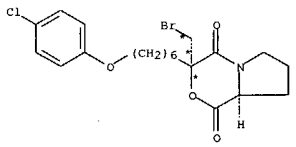
L3 ANSWER 4 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(5) OF 28 ...S ===> W...



S

(5)



W

RX(5) RCT S **468095-77-4**

STAGE(1)
RGT X 865-47-4 t-BuOK
SOL 68-12-2 DMF

STAGE(2)
RGT Y 128-08-5 Bromosuccinimide
SOL 68-12-2 DMF
PRO W **467235-26-3**

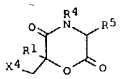
ACCESSION NUMBER: 137:294963 CASREACT
TITLE: Methods for producing oxirane carboxylic acids and derivatives thereof for use in treating hyperlipidemia
INVENTOR(S): Cernerud, Magnus; Berntsson, Kristina
PATENT ASSIGNEE(S): Medigene Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1

L3 ANSWER 4 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002079178	A1	20021010	WO 2002-EP3581	20020328
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10115938	A1	20021010	DE 2001-10115938	20010330
EP 1373237	A1	20040102	EP 2002-727511	20020328
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
US 2004236103	A1	20041125	US 2004-473503	20040524
PRIORITY APPLN. INFO.:			DE 2001-10115938	20010330
			WO 2002-EP3581	20020328

OTHER SOURCE(S): MARPAT 137:294963
GI

I



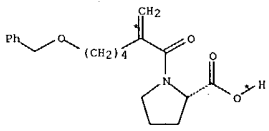
II

AB The invention relates to methods for producing oxirane carboxylic acids I [R1 = straight or branched (un)substituted alkyl, alkene, aralkyl, alkylaryl, aryl; R6 = OH] and derivs. I [R6 = O-M+, O-M2+, OR; M = alkali, alkaline earth, earth metal, ammonium cation, alkylated ammonium cation; R = (un)substituted C1-15-alkyl, -alkene] thereof via the morpholinediones II [R4, R5 = straight or branched (un)substituted alkyl, alkene, aralkyl, alkylaryl, aryl; R4NCR5 = (un)substituted heterocycle containing N, S, O; X4 = functional group, which is able to form a cationic intermediate in a reaction with a C-C double bond and is a good leaving group; with the proviso that R1 and R4NCR5 are not simultaneously R1 = (CH2)6OCH2Ph and R4NCR5 = a five-membered ring are not simultaneously], particularly to methods that are conducted under stereochem. control of the reaction steps, to the inventively produced oxirane carboxylic acids and derivs.

L3 ANSWER 4 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)
thereof, and to their use in pharmaceutical compns., particularly for treating hyperlipidemia. The synthesis of I contains the following steps:
(a) reaction of acrylic acid deriv., H2C:CR1CO2H, with amino acid, R4NHCHR5CO2H, to give the N-acylamino acid, R1C(:CH2)CONR4CHR5CO2H; (b) reaction of the latter to give lactone lactam I. Thus, (+)-etomixir was prepd. from.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

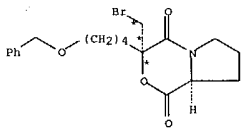
L3 ANSWER 5 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(5) OF 45 ...R ===> S...



R

(5)

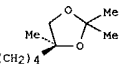


S
YIELD 60%

RX(5) RCT R **454439-61-3**
RGT T 128-08-5 Bromosuccinimide
PRO S **454439-62-4**
SOL 68-12-2 DMF
NTE stereoselective

ACCESSION NUMBER: 137:216896 CASREACT
TITLE: Asymmetric synthesis of (S)-4-(2,2,4-trimethyl-1,3-dioxolan-4-yl)-1-butanol, a key intermediate for (1S,5R)-(-)-frontalin via asymmetric bromolactonization
AUTHOR(S): Jew, Sang-sup; Lim, Doo-Yeon; Kim, Jin-Yee; Kim, Sung-ji; Roh, Eun-young; Yi, Hyo-Jeong; Ku, Jin-Mo; Park, Boon-saeng; Jeong, Byeong-seon; Park, Hyeung-geun
CORPORATE SOURCE: Research Institute of Pharmaceutical Science and College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Tetrahedron: Asymmetry (2002), 13(2), 155-159
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 5 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



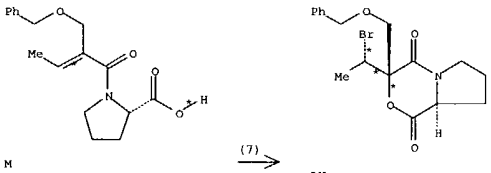
I

AB An asym. synthesis of (S)-4-(2,2,4-trimethyl-1,3-dioxolan-4-yl)-1-butanol (I), a key intermediate for (1S,5R)-(-)-frontalin, via asym. bromolactonization employing (S)-(-)-proline as a chiral auxiliary is described.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 6 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(7) OF 66 ...M ===> AK...



M (7) AK
YIELD 51%

RX(7) RCT M **326476-73-7**
RGT AL 128-08-5 Bromosuccinimide, X 109-72-8 BuLi
PRO AK **326476-75-9**
SOL 68-12-2 DMF
NTE stereoselective

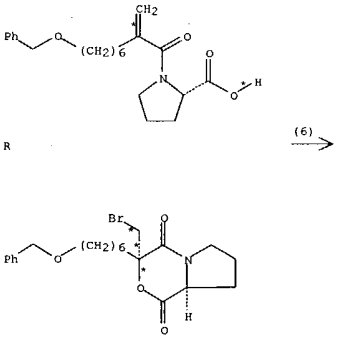
ACCESSION NUMBER: 134:178422 CASREACT
TITLE: Enantioselective synthesis of (S)-N,N-diethyl-2-formyl-2-(methoxymethoxy)butyramide, a key intermediate for 20(S)-camptothecin analogues, via asymmetric bromolactonization
AUTHOR(S): Jew, S.-s.; Roh, E.-y.; Kim, H.-j.; Goo Kim, M.; Park, H.-g.
CORPORATE SOURCE: College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Tetrahedron: Asymmetry (2000), 11(19), 3985-3994
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new enantioselective synthetic method for enantiomerically pure (S)-N,N-diethyl-2-formyl-2-(methoxymethoxy)butyramide, a versatile key intermediate, has been developed employing asym. bromolactonization using (S)-proline as the chiral auxiliary.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L3 ANSWER 7 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(6) OF 45 ...R ===> T...

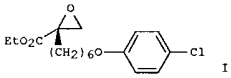


R (6) T
YIELD 87%

RX(6) RCT R **191412-51-8**
RGT U 128-08-5 Bromosuccinimide
PRO T **191412-52-9**
SOL 68-12-2 DMF

ACCESSION NUMBER: 127:65647 CASREACT
TITLE: Asymmetric synthesis of (R)-(+)-etomoxir
AUTHOR(S): Jew, Sang-Sup; Kim, Hyung-Ook; Jeong, Byeong-Seon; Park, Hyeung-Geun
CORPORATE SOURCE: College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Tetrahedron: Asymmetry (1997), 8(8), 1187-1192
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 7 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



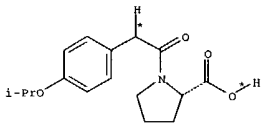
I

AB An asym. synthesis of etomoxir I, involving bromolactonization by using (S)-(-)-proline as a chiral auxiliary, is reported.

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

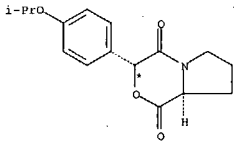
L3 ANSWER 8 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 5 2 F ===> G + H

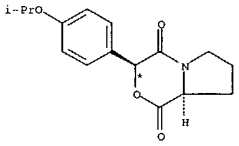


2 F

(2)



G



H

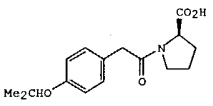
YIELD 80%(82)

YIELD 80%(18)

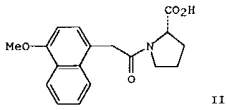
RX(2) RCT F **105988-50-9**
RGT D 84-58-2 DDQ
PRO G **105958-41-6**, H 106033-27-6
SOL 67-66-3 CHCl3
NTE stereoselective

ACCESSION NUMBER: 115:71509 CASREACT
TITLE: Asymmetric synthesis of heterocycles using charge transfer complex intermediates
AUTHOR(S): Lemaire, Marc; Guy, Alain; Imbert, Dominique; Guette, Jean Paul
CORPORATE SOURCE: Lab. Catal. Synth. Org., CNRS, Villeurbanne, 69622, Fr.
SOURCE: New Journal of Chemistry (1991), 15(5), 379-84
CODEN: NJCHE5; ISSN: 0398-9836
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

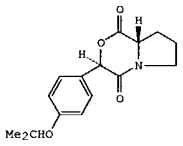
L3 ANSWER 8 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



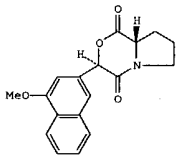
I



II



III

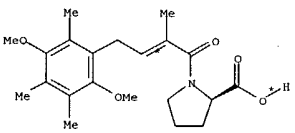


IV

AB Use of dichlorodicyanobenzoquinone (DDQ) as an oxidative reagent which performs donor-acceptor interactions with electron rich substrates, permits the diastereocontrol of heterocycle formation and thus the stereoselective synthesis of substituted morpholinediones. Thus, amides I and II, when treated with DDQ, gave 80% [65% diastereomer excess (d.e.)] morpholine III and 50% (40% d.e.) of morpholine IV, resp.

L3 ANSWER 9 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

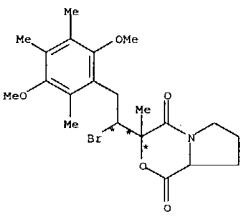
RX(4) OF 13 I ===> J...



● K

I

(4)

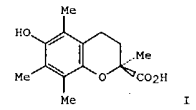


J

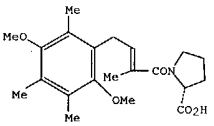
RX(4) RCT I **123294-79-1**
RGT K 128-08-5 Bromosuccinimide
PRO J **123294-77-9**

ACCESSION NUMBER: 111:195169 CASREACT
TITLE: Novel synthesis of (S)-(-)-chroman-2-carboxylic acid, a vitamin E precursor
AUTHOR(S): Yoda, Hidemi; Takabe, Kunihiko
CORPORATE SOURCE: Fac. Eng., Shizuoka Univ., Hamamatsu, 432, Japan
SOURCE: Chemistry Letters (1989), (3), 465-6
CODEN: CMLTAG; ISSN: 0366-7022
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 9 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



I

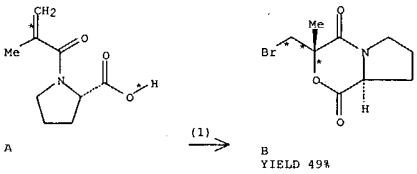


II

AB A new strategy for the synthesis of (S)-(-)-chroman-2-carboxylic acid I, a pivotal intermediate possessing the absolute configuration required for the construction of α-tocopherol, was disclosed by utilizing asym. halolactonization of acylproline II. Debromination followed by acidic hydrolysis directly afforded the title compound in 98% enantiomeric excess.

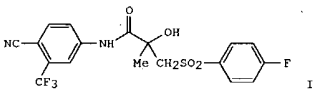
L3 ANSWER 10 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(1) OF 15 **A** ===> **B**...



A B
YIELD 49%

RX(1) RCT A **51161-88-7**
RGT C 128-08-5 Bromosuccinimide
PRO B **106089-19-4**
SOL 68-12-2 DMF
ACCESSION NUMBER: 108:150026 CASREACT
TITLE: Resolution of the non-steroidal antiandrogen 4'-cyano-3-(4-fluorophenylsulfonyl)-2-hydroxy-2-methyl-3'-(trifluoromethyl)propionanilide and the determination of the absolute configuration of the active enantiomer
AUTHOR(S): Tucker, Howard; Chesterson, Glynne J.
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind. PLC, Mereside/Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Journal of Medicinal Chemistry (1988), 31(4), 885-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

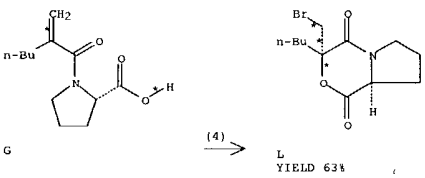
AB The nonsteroidal antiandrogen 4'-cyano-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-3'-(trifluoromethyl)propionanilide (I) has been resolved by chromatog. separation of the diastereomeric (R)-camphanyl esters of the precursor thioether followed by hydrolysis and oxidation of the isolated enantiomers. In addition, an asym. synthesis of (S)-3-bromo-2-hydroxy-2-

L3 ANSWER 10 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

methylpropanoic acid and subsequent conversion into the (S)-sulfone has established that the more potent enantiomer of I has the R abs. configuration.

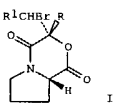
L3 ANSWER 11 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(4) OF 42 ...**G** ===> **L**...



G L
YIELD 63%

RX(4) RCT G **106089-16-1**
RGT M 128-08-5 Bromosuccinimide
PRO L **106089-17-2**
SOL 68-12-2 DMF
ACCESSION NUMBER: 107:236062 CASREACT
TITLE: Asymmetric bromolactonization reaction: synthesis of optically active 2-hydroxy-2-methylalkanoic acids from 2-methylenealkanoic acids
AUTHOR(S): Corey, Paul F.
CORPORATE SOURCE: Cent. Res. Serv. Div., Miles Lab., Inc., Elkhart, IN, 46515, USA
SOURCE: Tetrahedron Letters (1987), 28(25), 2801-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

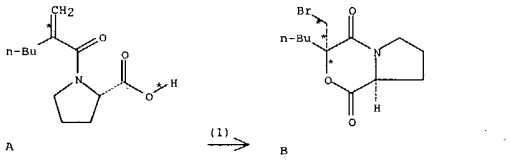


I

AB Acylation of L-proline with ClCOCR:CHR1 (R = H, R1 = Bu, Me; R = Bu, R1 = H), followed by bromolactonization with NBS gave bromolactones I. Debromination of I (R = H, R1 = Bu; R = Bu, R1 = H) with Bu3SnH, followed by hydrolysis, gave (R)- and (S)-HO2CCMeBuOH, resp. Hydrolysis of I (R = Me, R1 = H) gave optically active HO2CCMe(OH)CH2Br (II) in 88% yield. Reduction of II with BH3, protection with Me2C(OMe)2, alkylation with Pr2CuLi and hydrolysis gave (R)-HOCH2CMeBuOH.

L3 ANSWER 12 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(1) OF 1 **A** ===> **B**



A B

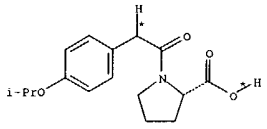
RX(1) RCT A **106089-16-1**
PRO B **106089-17-2**
ACCESSION NUMBER: 106:32692 CASREACT
TITLE: (+)-S-2-Hydroxy-2-methylhexanoic acid
INVENTOR(S): Corey, Paul Frederick
PATENT ASSIGNEE(S): Miles Laboratories, Inc., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 198348	A2	19861022	EP 1986-104583	19860404
EP 198348	A3	19880608		
EP 198348	B1	19900103		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1249842	A1	19890207	CA 1986-504794	19860324
AT 49193	E	19900115	AT 1986-104583	19860404
JP 61238757	A2	19861024	JP 1986-84436	19860414
US 4668822	A	19870526	US 1986-894390	19860811
PRIORITY APPLN. INFO.:			US 1985-723201	19850415
			EP 1986-104583	19860404

AB The title compound (+)-S-Me(CH2)3C(OH)MeCO2H (I), useful as an intermediate for 16-methyl-1,11α,16RS-trihydroxyprost-13E-en-9-one, was prepared via an asym. halolactonization reaction using L-proline as the chiral agent. Thus, 3S-methyl-3-butyl-1,4-dioxo-3,4,6,7,8,8aS-hexahydro-1H-pyrrolo[2,1-c]-1,4-oxazine, prepared in 3 steps from Me(CH2)3C(:CH2)COCl, was hydrolyzed with aqueous HBr to give I.

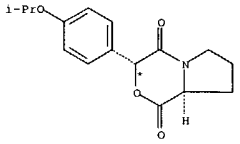
L3 ANSWER 13 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(3) OF 3 I ===> J + K

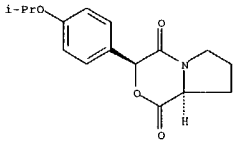


I

(3)



J



K

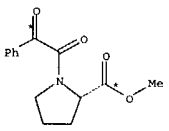
RX(3) RCT I **105988-50-9**
RGT D 84-58-2 DDQ
PRO J **105958-41-6**, K 106033-27-6
SOL 67-66-3 CHCl3
NTE diastereoselective

ACCESSION NUMBER: 106:32128 CASREACT
TITLE: Asymmetric control of oxidation of aromatic substrates using a donor-acceptor interaction
AUTHOR(S): Lemaire, Marc; Guy, Alain; Imbert, Dominique; Guette, Jean Paul
CORPORATE SOURCE: Lab. Chim. Org., Conserv. Natl. Arts Metiers, Paris, 75141, Fr.
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (10), 741-2
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English

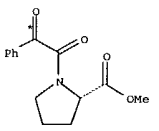
AB Asym. oxidation at the benzylic position of chiral aromatic substrates was controlled using a donor-acceptor interaction and DDQ as acceptor and oxidant. E.g., oxidn. of p-Me2CHOC6H4CH2CO2R [R = (-)-menthyl] with DDQ in AcOH at room temp. for 17 h gave a 6:4 diastereoisomeric mixt. of p-Me2CHOC6H4CH(OAc)CO2R in 90% yield.

L3 ANSWER 14 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

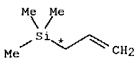
RX(2) OF 54 2 **G** + 2 B ===> **H** + I...



G

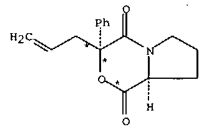


G

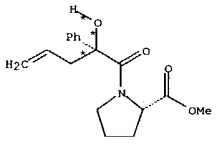


2 B

(2)



H

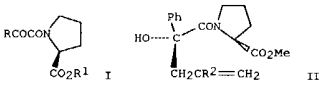


I

RX(2) RCT G **84653-73-6**, B 762-72-1
PRO H **103383-73-9**, I 94726-51-9
CAT 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

ACCESSION NUMBER: 105:134309 CASREACT
TITLE: Asymmetric synthesis of functionalized tertiary homoallyl alcohols by diastereoselective allylation of chiral α-keto amides derived from (S)-proline esters: control of stereochemistry based on saturated coordination of Lewis acid
AUTHOR(S): Soai, Kenso; Ishizaki, Miyuki
CORPORATE SOURCE: Fac. Sci., Sci. Univ. Tokyo, Tokyo, 162, Japan
SOURCE: Journal of Organic Chemistry (1986), 51(17), 3290-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 14 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

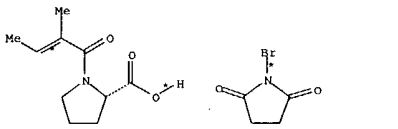


I II

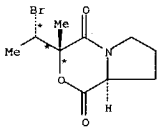
AB Diastereoselective addns. of allylsilanes and -stannanes to chiral α-keto amides I (R = Ph, R1 = Me, Me2CH; R = R1 = Me) derived from esters of (S)-proline in the presence of Lewis acids afforded optically active tertiary homoallyl alcs. of high diastereomeric excesses (up to 92% de). The order of the effectiveness of Lewis acids on diastereoselectivity was SnBr4 > SnCl4 > TiCl4 > BF3·OEt2 » AlCl3. At least 3 mol equiv of SnCl4 were required to achieve the high diastereoselection. The coordination of Lewis acids with the oxygen atom(s) of I may be one of the reasons for the high diastereoselectivity. When SnCl4 was used, CH2Cl2 was the best solvent. In the case of TiCl4, a heterogeneous reaction mixture in n-hexane and CH2Cl2 led to higher diastereoselectivity than a homogeneous solution in CH2Cl2 alone. Both allylsilane and -stannane led to homoallyl alcs. of predominant R configuration. The reaction was faster with allylstannane than with allylsilane. Allylation with allylmagnesium bromide showed the opposite diastereoselectivity. From a study of the effect of temperature, the enthalpy factor was found to be more important than the entropy factor. Some of the diastereomers (II; R2 = H, Me) cyclize spontaneously and stereoselectively to afford the corresponding lactones. The lactones were separated from the diastereomeric homoallyl alcs. by preparative TLC. Removal of the chiral auxiliaries by MeLi afforded essentially enantiomerically pure acyloins of both enantiomers.

L3 ANSWER 15 OF 15 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 11 E + B ===> F...



E B (2)

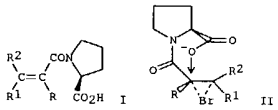


F

RX(2) RCT E **133694-86-7**, B 128-08-5
PRO F **65942-05-4**

ACCESSION NUMBER: 88:136919 CASREACT
TITLE: Novel aspects of the asymmetric bromolactonization reaction
AUTHOR(S): Terashima, Shiro; Jew, Sang-Sup; Koga, Kenji
CORPORATE SOURCE: Fac. Pharm. Sci., Univ. Tokyo, Tokyo, Japan
SOURCE: Chemistry Letters (1977), (9), 1109-12
CODEN: CMLTAG; ISSN: 0366-7022
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 15 OF 15 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



I II

AB The asym. bromolactonization of proline derivs. I (R, R1, R2 = H, Me) proceeded highly stereo- and regiospecifically through transition states, e.g. II.

CASREACT

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 DEC 2004 HIGHEST RN 798532-74-8
DICTIONARY FILE UPDATES: 15 DEC 2004 HIGHEST RN 798532-74-8

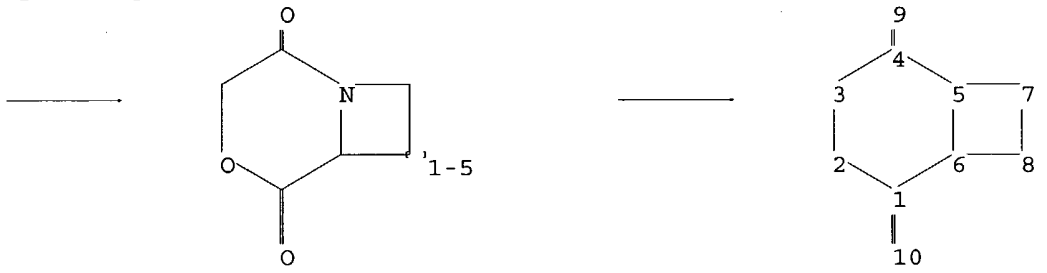
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10695048.str

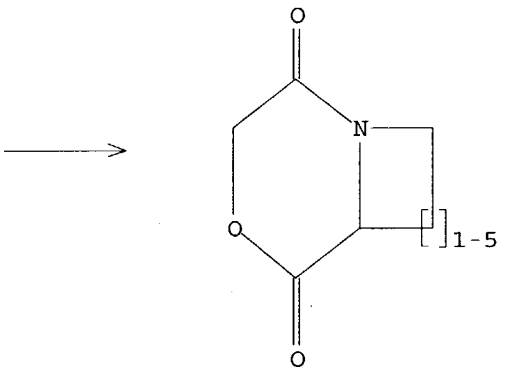


chain nodes :
9 10
ring nodes :
1 2 3 4 5 6 7 8
chain bonds :
1-10 4-9
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-8 7-8
exact/norm bonds :
1-2 1-6 1-10 2-3 3-4 4-5 4-9 5-6 5-7 6-8 7-8
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:CLASS 10:CLASS
fragments assigned product role:
containing 1

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



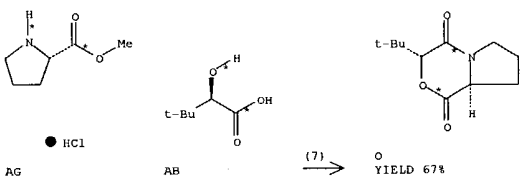
Structure attributes must be viewed using STN Express query preparation.

```
=> file casreact
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.42       0.63

FILE 'CASREACT' ENTERED AT 14:25:29 ON 17 DEC 2004
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.

FILE CONTENT:1840 - 12 Dec 2004 VOL 141 ISS 24

************************************************************
*                                                          *
*     CASREACT now has more than  8 million reactions      *
*                                                          *
************************************************************

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991)
provided by InfoChem, INPI data prior to 1986, and Biotransformations
database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance
identification.

=> s l1
SAMPLE SEARCH INITIATED 14:25:34 FILE 'CASREACT'
SCREENING COMPLETE -      1 REACTIONS TO VERIFY FROM      1 DOCUMENTS

100.0% DONE      1 VERIFIED       0 HIT RXNS                    0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED VERIFICATIONS:         1 TO       79
PROJECTED ANSWERS:               0 TO        0
```

```
L2            0 SEA SSS SAM L1 (      0 REACTIONS)

=> s l1 sss full
FULL SEARCH INITIATED 14:25:44 FILE 'CASREACT'
SCREENING COMPLETE -     427 REACTIONS TO VERIFY FROM      65 DOCUMENTS

100.0% DONE     427 VERIFIED      113 HIT RXNS                      19 DOCS
SEARCH TIME: 00.00.01

L3           19 SEA SSS FUL L1 (    113 REACTIONS)

=> d fhit ibib abs tot
```

L3 ANSWER 1 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(7) OF 129 ...AG + AB ===> O...



AG AB (7) O YIELD 67%

RX(7) RCT AG 2133-40-6

STAGE(1)
SOL 75-05-8 MeCN

STAGE(2)
RGT AH 7087-68-5 EtN(Pr-i)2

STAGE(3)
RCT AB 22146-57-2
RGT AI 2592-95-2 1-Benzotriazolol, AJ 25952-53-8 EDAP

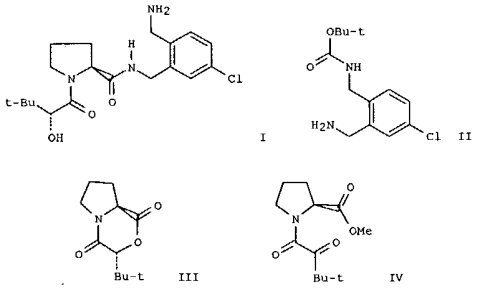
STAGE(4)
RGT U 7647-01-0 HCl
SOL 7732-18-5 Water

STAGE(5)
RGT AK 104-15-4 TsOH
SOL 108-88-3 PhMe
PRO O **685876-05-5**
NTE stereoselective

ACCESSION NUMBER: 141:88980 CASREACT
TITLE: Stereoselective Synthesis of a Potent Thrombin Inhibitor by a Novel P2-P3 Lactone Ring Opening
AUTHOR(S): Nelson, Todd D.; LeBlond, Carl R.; Frantz, Doug E.; Matty, Louis; Mitten, Jeffrey V.; Weaver, Damian G.; Moore, Jeffrey C.; Kim, Jaehon M.; Boyd, Russell; Kim, Pei-Yi; Gbewonyo, Kodzo; Brower, Mark; Sturr, Michael; McLaughlin, Kathleen; McMasters, Daniel R.; Kress, Michael H.; McNamara, James M.; Dolling, Ulf H.
CORPORATE SOURCE: Department of Process Research, Merck Research Laboratories, Merck & Co., Wayne, PA, 19087, USA
SOURCE: Journal of Organic Chemistry (2004), 69(11), 3620-3627

L3 ANSWER 1 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

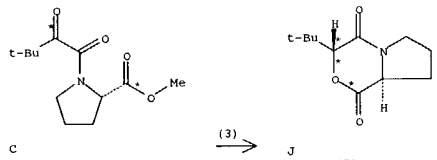


AB The concise synthesis of a potent thrombin inhibitor I·HBr was accomplished by a mild lactone aminolysis between an orthogonally protected bis-benzylic amine II and a diastereomerically pure lactone III. The lactone was synthesized by the condensation of L-proline Me ester with an enantiomerically pure 2-hydroxy-3,3-dimethylbutanoic acid, which in turn was synthesized by a highly stereoselective (>500:1 er) and productive (100000:1, S/C) enzymic reduction of corresponding α-ketoester followed by hydrolysis. In addition, a second route to the enantiomerically pure lactone III was accomplished via diastereoselective reduction of ketoamide IV.

REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(3) OF 5 ...C ===> J



C (3) J YIELD 67%

RX(3) RCT C 259173-97-2

STAGE(1)
RGT G 1333-74-0 H2
CAT 7440-18-8D Ru
SOL 67-56-1 MeOH

STAGE(2)
CAT 104-15-4 TsOH
SOL 108-88-3 PhMe
PRO J **685876-05-5**
NTE second stage stereoselective, other product detected

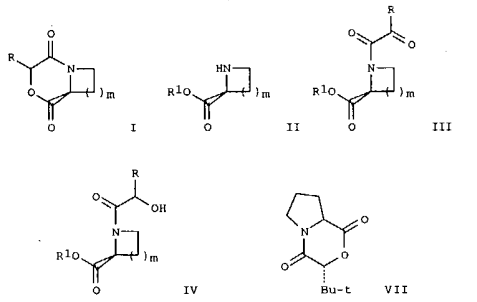
ACCESSION NUMBER: 140:391288 CASREACT
TITLE: Process of making N-heterocyclic bicyclic lactone compounds from ketoamides
INVENTOR(S): Nelson, Todd D.; Leblond, Carl; Mitten, Jeffrey V.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 9 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004087790	A1	20040506	US 2003-695048	20031028

PRIORITY APPLN. INFO.: US 2002-422701P 20021031
OTHER SOURCE(S): MARPAT 140:391288
GI

Own work

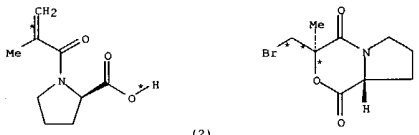
L3 ANSWER 2 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



AB Disclosed is a process of preparing a fused morpholine-2,5-dione [I; wherein R is (a) C 1-6 alkyl unsubstituted or substituted with one, two, or three groups independently selected from C 6-10 aryl, C 1-6 alkoxy, halogen, and amino; or (b) a 6-10 membered monocyclic or bicyclic aryl ring system, unsubstituted or substituted with one, two or three groups independently selected from C1-6 alkyl, C1-6 alkoxy, halogen, and amino group; and m is 1, 2, 3, 4, or 5] which comprises coupling a keto acid of formula RCOCO2H (R = same as above) with 1-azacycloalakane-2-carboxylic acid ester [II; R1 = (a) C1-6 alkyl unsubstituted or substituted with 1 to 3 groups independently selected from C6-10 aryl, HO, C1-6 alkoxy, halogen, and amino, (b) benzyl unsubstituted or substituted with one, two or three groups independently selected from C1-6 alkyl, hydroxy, C1-6 alkoxy, halogen, and amino, or (c) hydrogen], reducing the resulting ketoamides (III; R, R1, m = same as above), and cyclization of the resulting hydroxy ketoamides (IV; R, R1, m = same as above). Thus, 3,3-dimethyl-2-oxobutanoic acid was coupled with L-proline Me ester hydrochloride using HOBt/EDC as coupling reagents to give N-(3,3-dimethyl-2-oxobutanoyl)-L-proline Me ester (V) which was hydrogenated over 5% Ru/C in methanol at 50° and 40 psig H pressure for 71 h to give a crude mixture of N-[(R)- and (S)-3,3-dimethyl-2-hydroxybutanoyl)-L-proline Me ester (VI). VI was dissolved in toluene and stirred in the presence of p-MeC6H4SO3H at room temperature for 3 h under reduced pressure with removing methanol formed to give, after silica gel chromatog., lactone (VII) in 67% yield from V.

L3 ANSWER 3 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 15 ...C ===> G...



C (2) G YIELD 81%

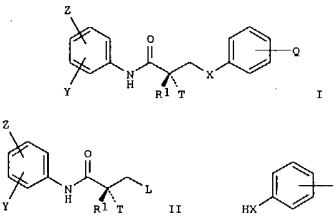
RX(2) RCT C 106089-24-1
RGT H 128-08-5 Bromosuccinimide
PRO G **106138-80-1**
SOL 68-12-2 DMF
NTE bromination and cyclization

ACCESSION NUMBER: 140:111132 CASREACT
TITLE: Method for preparation of N-[4-nitro-3-(trifluoromethyl)phenyl]-(2S)-3-[4-(acetylamino)phenoxy]-2-hydroxy-2-methylpropanamide and related compounds as selective androgen receptor modulators
INVENTOR(S): Dalton, James T.; Miller, Duane D.; He, Yali; Yin, Donghua
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 935,044.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004014975	A1	20040122	US 2002-277108	20021022
US 2002099036	A1	20020725	US 2001-935044	20010823
US 6492554	B2	20021210		
US 2002099096	A1	20020725	US 2001-935045	20010823
US 6569896	B2	20030527		
PRIORITY APPLN. INFO.:			US 2000-367355P	20000824
			US 2000-644970	20000824
			US 2001-300083P	20010625
			US 2001-935044	20010823
			US 2001-935045	20010823

OTHER SOURCE(S): MARPAT 140:111132
GI

L3 ANSWER 3 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



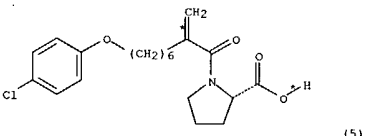
I

II III

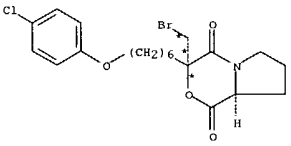
AB The present invention relates to a synthetic process for the preparation of a novel class of androgen receptor targeting agents (ARTA) [I; wherein X = O, NH, Se, PR, or NR; T = OH, OR, NHCOMe, NHCOR; Z = NO2, cyano, CO2H, COR, NHCOR, CONHR; Y = CF3, F, I, Br, Cl, cyano, CR3, SnR3; Q = alkyl, halogen, CF3, cyano, CR3, SnR3, NR2, NHCOMe, NHCOCF3, NHCOR, NHCONHR, NHCO2R, OCONHR, CONHR, NHCSMe, NHCSCF3, NHCSR NHSO2Me, NHSO2R, OR, COR, OCOR, OSO2R, SO2R, SR; or Q together with the benzene ring to which it is attached is a fused ring system represented by structure Q1, Q2 or Q3; R = alkyl, haloalkyl, dihaloalkyl, trihaloalkyl, CH2F, CHF2, CF3, CF2CF3, aryl, Ph, halogen, alkenyl, OH; R1 = Me, CH2F, CHF2, CF3, CH2CH3, CF2CF3] comprising the step of coupling an amide of formula (II) (Z, Y, R1, T = same as above; L = a leaving group) with a compound of formula (III) (Q, X = same as above). These agents demonstrate androgenic and anabolic activity of a nonsteroidal ligand for the androgen receptor (no data). The agents define a new subclass of compds. which are selective androgen receptor modulators (SARM) which are useful for (a) male contraception, (b) treatment of a variety of hormone-related conditions, for example conditions associated with androgen decline in aging male (ADAM), such as fatigue, depression, decreased libido, sexual dysfunction, erectile dysfunction, hypogonadism, osteoporosis, hair loss, anemia, obesity, sarcopenia, osteopenia, osteoporosis, benign prostate hyperplasia, alterations in mood and cognition and prostate cancer, (c) treatment of conditions associated with androgen decline in female (ADIF), such as sexual dysfunction, decreased sexual libido, hypogonadism, sarcopenia, osteopenia, osteoporosis, alterations in cognition and mood, depression, anemia, hair loss, obesity, endometriosis, breast cancer, uterine cancer and ovarian cancer, (d) treatment and/or prevention of chronic muscular wasting, (e) decreasing the incidence of, halting or causing a regression of prostate cancer, and (f) oral androgen replacement and/or other clin. therapeutic and/or diagnostic areas. The process of the present invention is suitable for large-scale prepn., since all of the steps give rise to highly pure compds., thus avoiding complicated purifn. procedures which ultimately lower the yield. Thus, the present invention provides methods for the synthesis of non-steroidal agonist compds., that can be used for industrial large-scale synthesis, and that provide highly pure products in high yield.

L3 ANSWER 4 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(5) OF 28 ...S ===> W...



S (5)



W

RX(5) RCT S 468095-77-4

STAGE(1)
RGT X 865-47-4 t-BuOK
SOL 68-12-2 DMF

STAGE(2)
RGT Y 128-08-5 Bromosuccinimide
SOL 68-12-2 DMF

PRO W **467235-26-3**

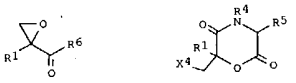
ACCESSION NUMBER: 137:294963 CASREACT
TITLE: Methods for producing oxirane carboxylic acids and derivatives thereof for use in treating hyperlipidemia
INVENTOR(S): Cernerud, Magnus; Berntsson, Kristina
PATENT ASSIGNEE(S): Medigene Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

L3 ANSWER 4 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

WO 2002079178 A1 20021010 WO 2002-EP3581 20020328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 10115938 A1 20021010 DE 2001-10115938 20010330
EP 1373237 A1 20040102 EP 2002-727511 20020328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2004236103 A1 20041125 US 2004-473503 20040524
PRIORITY APPLN. INFO.: DE 2001-10115938 20010330
WO 2002-EP3581 20020328

OTHER SOURCE(S): MARPAT 137:294963
GI



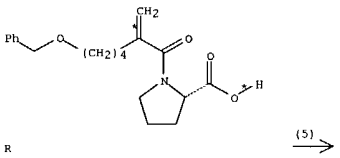
I II

AB The invention relates to methods for producing oxirane carboxylic acids I [R1 = straight or branched (un)substituted alkyl, alkene, aralkyl, alkylaryl, aryl; R6 = OH] and derivs. I [R6 = O-M+, O-M2+, OR; M = alkali, alkaline earth, earth metal, ammonium cation, alkylated ammonium cation; R = (un)substituted C1-15-alkyl, -alkene] thereof via the morpholinediones II [R4, R5 = straight or branched (un)substituted alkyl, alkene, aralkyl, alkylaryl, aryl; R4NCR5 = (un)substituted heterocycle containing N, S, O; X4 = functional group, which is able to form a cationic intermediate in a reaction with a C-C double bond and is a good leaving group; with the proviso that R1 and R4NCR5 are not simultaneously R1 = (CH2)6OCH2Ph and R4NCR5 = a five-membered ring are not simultaneously], particularly to methods that are conducted under stereochem. control of the reaction steps, to the inventively produced oxirane carboxylic acids and derivs. thereof, and to their use in pharmaceutical compns., particularly for treating hyperlipidemia. The synthesis of I contains the following steps:
(a) reaction of acrylic acid derivative, H2C:CR1CO2H, with amino acid, R4NHCHR5CO2H, to give the N-acylamino acid, R1C(:CH2)CONR4CHR5CO2H; (b) reaction of the latter to give lactone lactam I. Thus, (+)-etomixir was prepd. from.

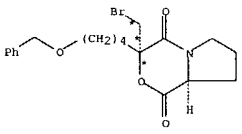
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(5) OF 45 ...R ===> S...



R (5)

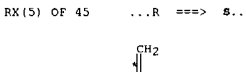


S
YIELD 60%

RX(5) RCT R 454439-61-3
RGT T 128-08-5 Bromosuccinimide
PRO S **454439-62-4**
SOL 68-12-2 DMF
NTE stereoselective

ACCESSION NUMBER: 137:216896 CASREACT
TITLE: Asymmetric synthesis of (S)-4-(2,2,4-trimethyl-1,3-dioxolan-4-yl)-1-butanol, a key intermediate for (1S,5R)-(-)-frontalin via asymmetric bromolactonization
AUTHOR(S): Jew, Sang-sup; Lim, Doo-Yeon; Kim, Jin-Yee; Kim, Sung-ji; Roh, Eun-young; Yi, Hyo-Jeong; Ku, Jin-Mo; Park, Boon-saeng; Jeong, Byeong-seon; Park, Hyeung-geun
CORPORATE SOURCE: Research Institute of Pharmaceutical Science and College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Tetrahedron: Asymmetry (2002), 13(2), 155-159
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 5 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



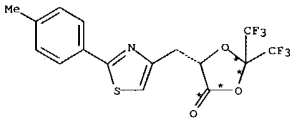
I

AB An asym. synthesis of (S)-4-(2,2,4-trimethyl-1,3-dioxolan-4-yl)-1-butanol (I), a key intermediate for (1S,5R)-(-)-frontalin, via asym. bromolactonization employing (S)-(-)-proline as a chiral auxiliary is described.

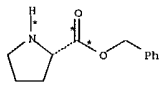
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(29) OF 141 ...N + BA ===> **BB**

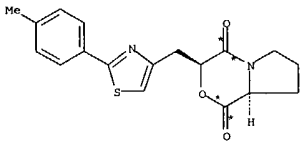


N



BA

(29)



BB
YIELD 58%

RX(29) RCT N 150582-59-5

STAGE(1)
SOL 60-29-7 Et2O

STAGE(2)
RCT BA 41324-66-7
SOL 60-29-7 Et2O
PRO BB **150582-49-3**
NTE stereoselective

ACCESSION NUMBER: 137:47145 CASREACT
TITLE: A preparatively simple access to homochiral heterocyclic α-hydroxy acids and their derivatives
AUTHOR(S): Burger, Klaus; Windeisen, Elisabeth; Heistracher, H.
CORPORATE SOURCE: Department of Organic Chemistry, University of Leipzig, Leipzig, D-04103, Germany
SOURCE: Monatshefte fuer Chemie (2002), 133(1), 41-58 / CODEN: MOCMB7; ISSN: 0026-9247
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

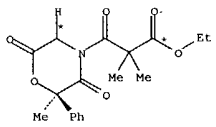
L3 ANSWER 6 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. I [R = H, 4-MeC6H4, 4-FC6H4, 4-ClC6H4, 2-furyl, 2-thienyl, 2-(p-tolyl)-4-(trifluoromethyl)-5-thiazolyl, PhNMe; R1 = HO, MeO, HONH, H2N, PhCH2NH] were prepared stereoselectively from the malic acid-hexafluoroacetone condensation product II (R2 = HO) via conversion to the bromomethyl ketone II (R2 = BrCH2), cyclocondensation with RC(S)NH2 to give thiazoles III, and finally deprotection with R1H. Analogous deprotection with amino acid derivs. results in formation of di- and tri-peptidomimetics. Thus, reaction of III (R = 4-FC6H4) with H-Ala-OCMe3 gave 66% lactoylalanine IV.
REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

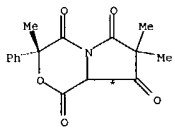
L3 ANSWER 7 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(4) OF 28 ...P ===> **R**...



P

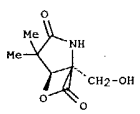
(4)



R
YIELD 87%

RX(4) RCT P 342797-11-9
RGT Q 121-44-8 Et3N, S 7550-45-0 TiCl4, T 75-77-4 Me3SiCl
PRO R **342797-12-0**
SOL 75-09-2 CH2Cl2
NTE Dieckmann reaction

ACCESSION NUMBER: 135:19883 CASREACT
TITLE: A Novel Enantioselective Synthetic Route to Omuralide Analogues with the Potential for Species Selectivity in Proteasome Inhibition
AUTHOR(S): Crane, Sheldon N.; Corey, E. J.
CORPORATE SOURCE: Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA, 02138, USA
SOURCE: Organic Letters (2001), 3(9), 1395-1397 / CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

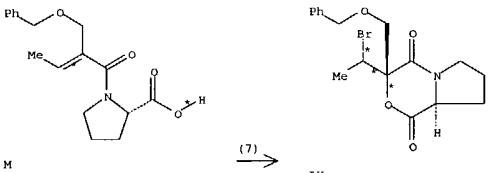
II

L3 ANSWER 7 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

AB The authors have developed a route for an enantioselective construction of the simplified omuralide analog I in nine steps, with the use of (R)-atrolactic acid (II) as a recoverable chiral controller.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(7) OF 66 ...M ===> **AK**...

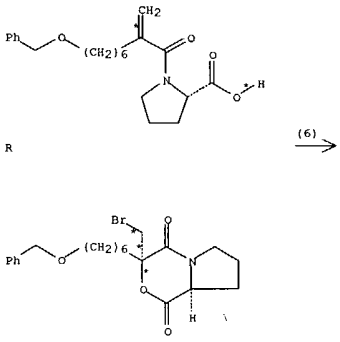


M (7) AK
YIELD 51%

RX(7) RCT M 326476-73-7
RGT AL 128-08-5 Bromosuccinimide, X 109-72-8 BuLi
PRO AK **326476-75-9**
SOL 68-12-2 DMF
NTE stereoselective
ACCESSION NUMBER: 134:178422 CASREACT
TITLE: Enantioselective synthesis of (S)-N,N-diethyl-2-formyl-2-(methoxymethoxy)butyramide, a key intermediate for 20(S)-camptothecin analogues, via asymmetric bromolactonization
AUTHOR(S): Jew, S.-s.; Roh, E.-y.; Kim, H.-j.; Goo Kim, M.; Park, H.-g.
CORPORATE SOURCE: College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Tetrahedron: Asymmetry (2000), 11(19), 3985-3994
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new enantioselective synthetic method for enantiomerically pure (S)-N,N-diethyl-2-formyl-2-(methoxymethoxy)butyramide, a versatile key intermediate, has been developed employing asym. bromolactonization using (S)-proline as the chiral auxiliary.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

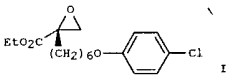
RX(6) OF 45 ...R ===> **T**...



R (6) T
YIELD 87%

RX(6) RCT R 191412-51-8
RGT U 128-08-5 Bromosuccinimide
PRO T **191412-52-9**
SOL 68-12-2 DMF
ACCESSION NUMBER: 127:65647 CASREACT
TITLE: Asymmetric synthesis of (R)-(+)-etomoxir
AUTHOR(S): Jew, Sang-Sup; Kim, Hyung-Ook; Jeong, Byeong-Seon; Park, Hyeung-Geun
CORPORATE SOURCE: College of Pharmacy, Seoul National University, Seoul, 151-742, S. Korea
SOURCE: Tetrahedron: Asymmetry (1997), 8(8), 1187-1192
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 9 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

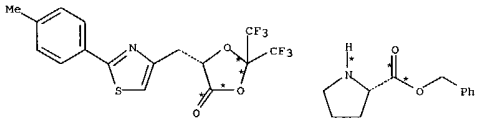


I

AB An asym. synthesis of etomoxir I, involving bromolactonization by using (S)-(-)-proline as a chiral auxiliary, is reported.
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

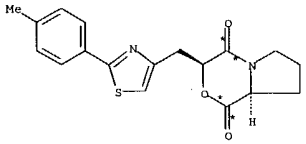
L3 ANSWER 10 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(4) OF 4 K + L ===> **M**



K L

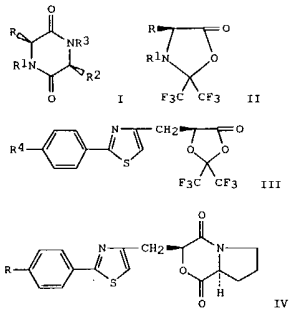
(4)



M
YIELD 58%

RX(4) RCT K 150582-59-5, L 41324-66-7
PRO M **150582-49-3**
SOL 60-29-7 Et2O
ACCESSION NUMBER: 119:226381 CASREACT
TITLE: Hexafluoroacetone as protecting group and activating reagent in amino acid and peptide chemistry. XI. A new simple preparative access to 2,5-dioxopiperazines and 2,5-dioxomorpholines
AUTHOR(S): Burger, K.; Rudolph, M.; Windeisen, E.; Worku, A.; Fehn, S.
CORPORATE SOURCE: Org.-Chem. Inst., Tech. Univ. Muenchen, Garching, W-8046, Germany
SOURCE: Monatshefte fuer Chemie (1993), 124(4), 453-63
CODEN: MOCMB7; ISSN: 0026-9247
DOCUMENT TYPE: Journal
LANGUAGE: German
GI

L3 ANSWER 10 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

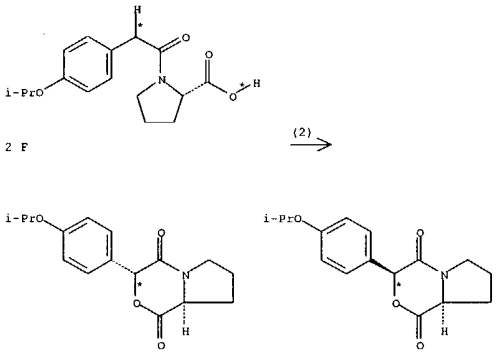


I II III IV

AB 2,5-Dioxopiperazines I [R = R2 = Me,CH2C6H4OH-4,CH2OH, CHMeOH, R1 = R3 = H; R = R2 = H, R1 = R3 = Me; RR1 = R2R3 = (CH2)3] were obtained by dimerizing the oxazolidines II in MeOH at room temperature I (R, R2 = different amino acid residues, R1, R3 = H) were obtained from II and R3NHCHR2CO2Me. The dioxolanes III (R4 = Me, F, Cl) similarly gave the morpholines IV.

L3 ANSWER 11 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 5 2 F ===> G + H



2 F (2)

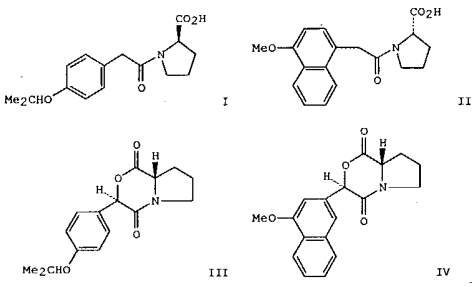
G YIELD 80%(82)

H YIELD 80%(18)

RX(2) RCT F 105988-50-9
RGT D 84-58-2 DDQ
PRO G **105958-41-6**, H 106033-27-6
SOL 67-66-3 CHCl3
NTE stereoselective

ACCESSION NUMBER: 115:71509 CASREACT
TITLE: Asymmetric synthesis of heterocycles using charge transfer complex intermediates
AUTHOR(S): Lemaire, Marc; Guy, Alain; Imbert, Dominique; Guette, Jean Paul
CORPORATE SOURCE: Lab. Catal. Synth. Org., CNRS, Villeurbanne, 69622, Fr.
SOURCE: New Journal of Chemistry (1991), 15(5), 379-84
CODEN: NJCHE5; ISSN: 0398-9836
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 11 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

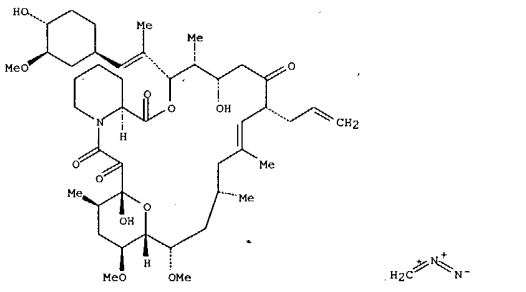


I II III IV

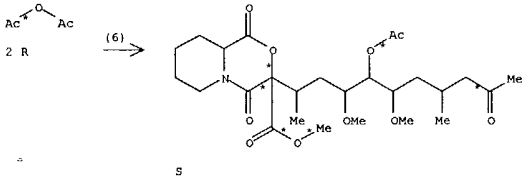
AB Use of dichlorodicyanobenzoquinone (DDQ) as an oxidative reagent which performs donor-acceptor interactions with electron rich substrates, permits the diastereocontrol of heterocycle formation and thus the stereoselective synthesis of substituted morpholinediones. Thus, amides I and II, when treated with DDQ, gave 80% [65% diastereomer excess (d.e.)] morpholine III and 50% (40% d.e.) of morpholine IV, resp.

L3 ANSWER 12 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(6) OF 14 A + K + 2 R ===> S



A K



2 R (6)

S

RX(6) RCT A 104987-11-3

STAGE(1)
RGT T 1310-73-2 NaOH
SOL 7732-18-5 Water, 123-91-1 Dioxane

STAGE(2)
RCT K 334-88-3

STAGE(3)
RCT R 108-24-7
SOL 110-86-1 Pyridine

L3 ANSWER 12 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

STAGE(4)
RGT U 10028-15-6 Ozone
PRO S **123719-20-0**

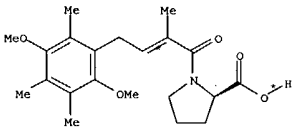
ACCESSION NUMBER: 111:232396 CASREACT
TITLE: Chemistry of FK-506: benzilic acid rearrangement of the tricarbonyl system
AUTHOR(S): Askin, D.; Reamer, R. A.; Jones, T. K.; Volante, R. P.; Shinkai, I.
CORPORATE SOURCE: Dep. Process Res., Merck Sharp and Dohme Res. Lab., Rahway, NJ, 07065, USA
SOURCE: Tetrahedron Letters (1989), 30(6), 671-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Treatment of FK-506 (I) with aqueous hydroxide results in a benzilic acid rearrangement of the C(8)-C(10) tricarbonyl portion of the mol. A corrected structure II for a previously reported degradation product as well as oxidative decarboxylation of rearranged FK-506 is presented.

L3 ANSWER 13 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

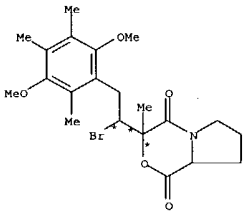
RX(4) OF 13 I ===> J...



● K

I

(4) ⟶



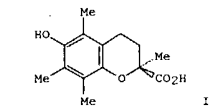
J

RX(4) RCT I 123294-79-1
RGT K 128-08-5 Bromosuccinimide
PRO J **123294-77-9**

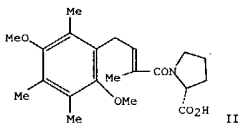
ACCESSION NUMBER: 111:195169 CASREACT
TITLE: Novel synthesis of (S)-(-)-chroman-2-carboxylic acid, a vitamin E precursor
AUTHOR(S): Yoda, Hidemi; Takabe, Kunihiko
CORPORATE SOURCE: Fac. Eng., Shizuoka Univ., Hamamatsu, 432, Japan
SOURCE: Chemistry Letters (1989), (3), 465-6
CODEN: CMLTAG; ISSN: 0366-7022
DOCUMENT TYPE: Journal
LANGUAGE: English

L3 ANSWER 13 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

GI



I

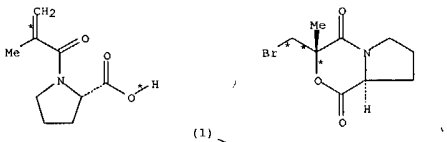


II

AB A new strategy for the synthesis of (S)-(-)-chroman-2-carboxylic acid I, a pivotal intermediate possessing the absolute configuration required for the construction of α-tocopherol, was disclosed by utilizing asym. halolactonization of acylproline II. Debromination followed by acidic hydrolysis directly afforded the title compound in 98% enantiomeric excess.

L3 ANSWER 14 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(1) OF 15 A ===> B...



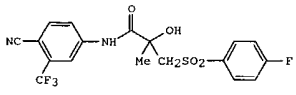
A

(1) ⟶

B
YIELD 49%

RX(1) RCT A 51161-88-7
RGT C 128-08-5 Bromosuccinimide
PRO B **106089-19-4**
SOL 68-12-2 DMF

ACCESSION NUMBER: 108:150026 CASREACT
TITLE: Resolution of the non-steroidal antiandrogen 4'-cyano-3-(4-fluorophenylsulfonyl)-2-hydroxy-2-methyl-3'-(trifluoromethyl)propionanilide and the determination of the absolute configuration of the active enantiomer
AUTHOR(S): Tucker, Howard; Chesterson, Glynne J.
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind. PLC, Mereside/Macclesfield/Cheshire, SK10 4TG, UK
SOURCE: Journal of Medicinal Chemistry (1988), 31(4), 885-7
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



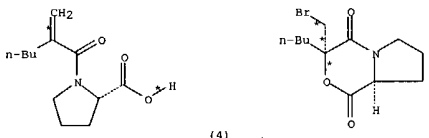
I

AB The nonsteroidal antiandrogen 4'-cyano-3-[(4-fluorophenyl)sulfonyl]-2-hydroxy-2-methyl-3'-(trifluoromethyl)propionanilide (I) has been resolved by chromatog. separation of the diastereomeric (R)-camphanyl esters of the precursor thioether followed by hydrolysis and oxidation of the isolated enantiomers. In addition, an asym. synthesis of (S)-3-bromo-2-hydroxy-2-methylpropanoic acid and subsequent conversion into the (S)-sulfone has established that the more potent enantiomer of I has the R absolute configuration.

L3 ANSWER 14 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

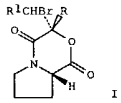
L3 ANSWER 15 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(4) OF 42 ...G ===> L...



G (4) L
YIELD 63%

RX(4) RCT G 106089-16-1
RGT M 128-08-5 Bromosuccinimide
PRO L **106089-17-2**
SOL 68-12-2 DMF
ACCESSION NUMBER: 107:236062 CASREACT
TITLE: Asymmetric bromolactonization reaction: synthesis of optically active 2-hydroxy-2-methylalkanoic acids from 2-methylenealkanoic acids
AUTHOR(S): Corey, Paul F.
CORPORATE SOURCE: Cent. Res. Serv. Div., Miles Lab., Inc., Elkhart, IN, 46515, USA
SOURCE: Tetrahedron Letters (1987), 28(25), 2801-4
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



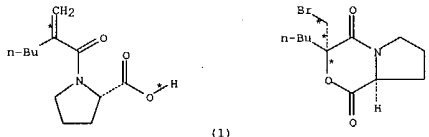
I

AB Acylation of L-proline with ClCOCR:CHR1 (R = H, R1 = Bu, Me; R = Bu, R1 = H), followed by bromolactonization with NBS gave bromolactones I. Debromination of I (R = H, R1 = Bu; R = Bu, R1 = H) with Bu3SnH, followed by hydrolysis, gave (R)- and (S)-HO2CCMeBuOH, resp. Hydrolysis of I (R = Me, R1 = H) gave optically active HO2CCMe(OH)CH2Br (II) in 88% yield. Reduction of II with BH3, protection with Me2C(OMe)2, alkylation with Pr2CuLi and hydrolysis gave (R)-HOCH2CMeBuOH.

L3 ANSWER 15 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

L3 ANSWER 16 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(1) OF 1 A ===> B



A (1) B

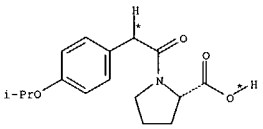
RX(1) RCT A 106089-16-1
PRO B **106089-17-2**
ACCESSION NUMBER: 106:32692 CASREACT
TITLE: (+)-S-2-Hydroxy-2-methylhexanoic acid
INVENTOR(S): Corey, Paul Frederick
PATENT ASSIGNEE(S): Miles Laboratories, Inc., USA
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 198348	A2	19861022	EP 1986-104583	19860404
EP 198348	A3	19880608		
EP 198348	B1	19900103		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
CA 1249842	A1	19890207	CA 1986-504794	19860324
AT 49193	E	19900115	AT 1986-104583	19860404
JP 61238757	A2	19861024	JP 1986-84436	19860414
US 4668822	A	19870526	US 1986-894390	19860811
PRIORITY APPLN. INFO.:			US 1985-723201	19850415
			EP 1986-104583	19860404

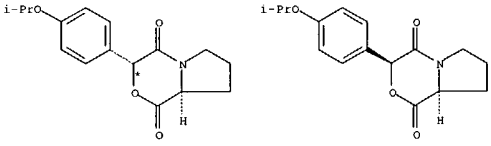
AB The title compound (+)-S-Me(CH2)3C(OH)MeCO2H (I), useful as an intermediate for 16-methyl-1,11α,16RS-trihydroxyprost-13E-en-9-one, was prepared via an asym. halolactonization reaction using L-proline as the chiral agent. Thus, 3S-methyl-3-butyl-1,4-dioxo-3,4,6,7,8,8αS-hexahydro-1H-pyrrolo[2,1-c]-1,4-oxazine, prepared in 3 steps from Me(CH2)3C(:CH2)COCl, was hydrolyzed with aqueous HBr to give I.

L3 ANSWER 17 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(3) OF 3 I ===> J + K



I



J K

RX(3) RCT I 105988-50-9
RGT D 84-58-2 DDQ
PRO J **105958-41-6**, K 106033-27-6
SOL 67-66-3 CHCl3
NTE diastereoselective

ACCESSION NUMBER: 106:32128 CASREACT
TITLE: Asymmetric control of oxidation of aromatic substrates using a donor-acceptor interaction
AUTHOR(S): Lemaire, Marc; Guy, Alain; Imbert, Dominique; Guette, Jean Paul
CORPORATE SOURCE: Lab. Chim. Org., Conserv. Natl. Arts Metiers, Paris, 75141, Fr.
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (10), 741-2
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English

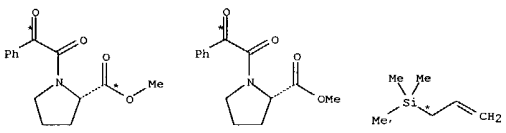
AB Asym. oxidation at the benzylic position of chiral aromatic substrates was

L3 ANSWER 17 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

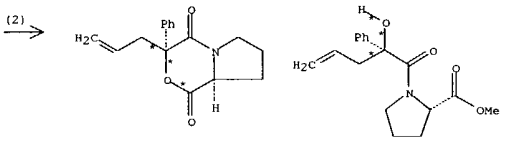
controlled using a donor-acceptor interaction and DDQ as acceptor and oxidant. E.g., oxidn. of p-Me2CHOC6H4CH2CO2R [R = (-)-menthyl] with DDQ in AcOH at room temp. for 17 h gave a 6:4 diastereoisomeric mixt. of p-Me2CHOC6H4CH(OAc)CO2R in 90% yield.

L3 ANSWER 18 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 54 2 G + 2 B ===> H + I...



G G 2 B

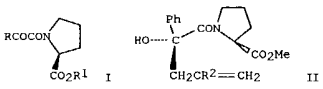


H I

RX(2) RCT G 84653-73-6, B 762-72-1
PRO H **103383-73-9**, I 94726-51-9
CAT 7550-45-0 TiCl4
SOL 75-09-2 CH2Cl2

ACCESSION NUMBER: 105:134309 CASREACT
TITLE: Asymmetric synthesis of functionalized tertiary homoallyl alcohols by diastereoselective allylation of chiral α-keto amides derived from (S)-proline esters: control of stereochemistry based on saturated coordination of Lewis acid
AUTHOR(S): Soai, Kenso; Ishizaki, Miyuki
CORPORATE SOURCE: Fac. Sci., Sci. Univ. Tokyo, Tokyo, 162, Japan
SOURCE: Journal of Organic Chemistry (1986), 51(17), 3290-5
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 18 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)

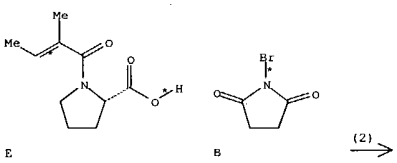


I II

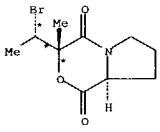
AB Diastereoselective addns. of allylsilanes and -stannanes to chiral α-keto amides I (R = Ph, R1 = Me, Me2CH; R = R1 = Me) derived from esters of (S)-proline in the presence of Lewis acids afforded optically active tertiary homoallyl alcs. of high diastereomeric excesses (up to 92% de). The order of the effectiveness of Lewis acids on diastereoselectivity was SnBr4 > SnCl4 > TiCl4 > BF3·OEt2 » AlCl3. At least 3 mol equiv of SnCl4 were required to achieve the high diastereoselection. The coordination of Lewis acids with the oxygen atom(s) of I may be one of the reasons for the high diastereoselectivity. When SnCl4 was used, CH2Cl2 was the best solvent. In the case of TiCl4, a heterogeneous reaction mixture in n-hexane and CH2Cl2 led to higher diastereoselectivity than a homogeneous solution in CH2Cl2 alone. Both allylsilane and -stannane led to homoallyl alcs. of predominant R configuration. The reaction was faster with allylstannane than with allylsilane. Allylation with allylmagnesium bromide showed the opposite diastereoselectivity. From a study of the effect of temperature, the enthalpy factor was found to be more important than the entropy factor. Some of the diastereomers (II; R2 = H, Me) cyclize spontaneously and stereoselectively to afford the corresponding lactones. The lactones were separated from the diastereomeric homoallyl alcs. by preparative TLC. Removal of the chiral auxiliaries by MeLi afforded essentially enantiomerically pure acyloins of both enantiomers.

L3 ANSWER 19 OF 19 CASREACT COPYRIGHT 2004 ACS on STN

RX(2) OF 11 E + B ===> F...



E B (2)

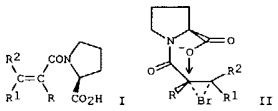


F

RX(2) RCT E 133694-86-7, B 128-08-5
PRO F **65942-05-4**

ACCESSION NUMBER: 88:136919 CASREACT
TITLE: Novel aspects of the asymmetric bromolactonization reaction
AUTHOR(S): Terashima, Shiro; Jew, Sang-Sup; Koga, Kenji
CORPORATE SOURCE: Fac. Pharm. Sci., Univ. Tokyo, Tokyo, Japan
SOURCE: Chemistry Letters (1977), (9), 1109-12
CODEN: CMLTAG; ISSN: 0366-7022
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

L3 ANSWER 19 OF 19 CASREACT COPYRIGHT 2004 ACS on STN (Continued)



I II

AB The asym. bromolactonization of proline derivs. I (R, R1, R2 = H, Me) proceeded highly stereo- and regiospecifically through transition states, e.g. II.